

WE CLAIM:

1. A method of inducing osteoblastic differentiation of mammalian mesenchymal stem cells including treating mammalian mesenchymal cells with at least one oxysterol.

2. The method of claim 1, wherein the at least one oxysterol is selected from the group comprising 20S-hydroxycholesterol, 22S-hydroxycholesterol, 22R-hydroxycholesterol, 25-hydroxycholesterol, or pregnanolone, or an active portion of any one of 20S-hydroxycholesterol, 22S-hydroxycholesterol, 22R-hydroxycholesterol, 25-hydroxycholesterol, or pregnanolone.

3. The method of claim 1, wherein the at least one oxysterol is a combination of oxysterols selected from the group comprising 20S-hydroxycholesterol and 22R-hydroxycholesterol, or 20S-hydroxycholesterol and 22S-hydroxycholesterol.

4. The method of claim 1, further comprising treating the mammalian mesenchymal cells with at least one secondary agent selected from the group comprising parathyroid hormone, sodium fluoride, insulin-like growth factor I, insulin-like growth factor II or transforming growth factor beta.

5. The method of claim 1, further comprising treating the mammalian mesenchymal cells with at least one secondary agent selected from the group comprising cytochrome P450 inhibitors, phospholipase activators, arachadonic acid, COX enzyme activators, osteogenic prostanoids or ERK activators.

6. A method of stimulating mammalian cells to express a level of a biological marker of osteoblastic differentiation which is greater than the level of a biological marker in untreated cells, comprising exposing a mammalian cell to a selected dose of at least one oxysterol.

7. The method of claim 6, wherein the at least one oxysterol is selected from the group comprising 20S-hydroxycholesterol, 22S-hydroxycholesterol, 22R-hydroxycholesterol, 25-hydroxycholesterol, or pregnanolone, or an active portion of any one of 20S-hydroxycholesterol, 22S-

hydroxycholesterol, 22R-hydroxycholesterol, 25-hydroxycholesterol, or pregnanolone.

8. The method of claim 6, wherein the at least one oxysterol is a combination of oxysterols selected from the group comprising 20S-hydroxycholesterol and 22R-hydroxycholesterol, or 20S-hydroxycholesterol and 22S-hydroxycholesterol.

9. The method of claim 6, further comprising treating the mammalian mesenchymal cells with at least one secondary agent selected from the group comprising parathyroid hormone, sodium fluoride, insulin-like growth factor I, insulin-like growth factor II or transforming growth factor beta.

10. The method of claim 6, further comprising treating the mammalian mesenchymal cells with at least one secondary agent selected from the group comprising cytochrome P450 inhibitors, phospholipase activators, arachadonic acid, COX enzyme activators, osteogenic prostanoids or ERK activators.

11. The method of claim 6 wherein the biological marker is an increase in at least one of alkaline phosphatase activity, calcium incorporation, mineralization or expression of osteocalcin mRNA.

12. The method of claim 6 wherein the mammalian cells are selected from the group comprising mesenchymal stem cells, osteoprogenitor cells or calvarial organ cultures.

13. A method of inhibiting adipocyte differentiation of mammalian mesenchymal stem cells including treating mammalian mesenchymal cells with at least one oxysterol.

14. The method of claim 13, wherein the at least one oxysterol is selected from the group comprising 20S-hydroxycholesterol, 22S-hydroxycholesterol, 22R-hydroxycholesterol, 25-hydroxycholesterol, or pregnanolone, or an active portion of any one of 20S-hydroxycholesterol, 22S-hydroxycholesterol, 22R-hydroxycholesterol, 25-hydroxycholesterol, or pregnanolone.

15. A method of treating a patient to increase the differentiation of marrow stromal cells into osteoblasts, comprising administering at least one oxysterol at a therapeutically effective dose in an effective dosage form at a selected interval to increase the number of osteoblasts present in bone tissue.

16. The method of claim 15, wherein the at least one oxysterol is selected from the group comprising 20S-hydroxycholesterol, 22S-hydroxycholesterol, 22R-hydroxycholesterol, 25-hydroxycholesterol, or pregnanolone, or an active portion of any one of 20S-hydroxycholesterol, 22S-hydroxycholesterol, 22R-hydroxycholesterol, 25-hydroxycholesterol, or pregnanolone.

17. The method of claim 15, wherein the at least one oxysterol is a combination of oxysterols selected from the group comprising 20S-hydroxycholesterol and 22R-hydroxycholesterol, or 20S-hydroxycholesterol and 22S-hydroxycholesterol.

18. The method of claim 15, further comprising treating the patient with at least one secondary agent selected from the group comprising parathyroid hormone, sodium fluoride, insulin-like growth factor I, insulin-like growth factor II or transforming growth factor beta.

19. A method of treating a patient to induce bone formation comprising administering at least one oxysterol at a therapeutically effective dose in an effective dosage form at a selected interval to increase bone mass.

20. The method of claim 19, wherein the at least one oxysterol is selected from the group comprising 20S-hydroxycholesterol, 22S-hydroxycholesterol, 22R-hydroxycholesterol, 25-hydroxycholesterol, or pregnanolone, or an active portion of any one of 20S-hydroxycholesterol, 22S-hydroxycholesterol, 22R-hydroxycholesterol, 25-hydroxycholesterol, or pregnanolone.

21. The method of claim 19, wherein the at least one oxysterol is a combination of oxysterols selected from the group comprising 20S-

hydroxycholesterol and 22R-hydroxycholesterol, or 20S-hydroxycholesterol and 22S-hydroxycholesterol.

22. The method of claim 19, further comprising treating the patient with at least one secondary agent selected from the group comprising parathyroid hormone, sodium fluoride, insulin-like growth factor I, insulin-like growth factor II or transforming growth factor beta, at a therapeutically effective dose.

23. A method of claim 19, further comprising treating a patient with at least one secondary agent selected from the group comprising bisphosphonates, selective estrogen receptor modulators, calcitonin, or vitamin D and calcium, at a therapeutically effective dose.

24. A method of treating a patient exhibiting clinical symptoms of osteoporosis comprising administering at least one oxysterol at a therapeutically effective dose in an effective dosage form at a selected interval to ameliorate the symptoms of the osteoporosis.

25. The method of claim 24, wherein the at least one oxysterol is selected from the group comprising 20S-hydroxycholesterol, 22S-hydroxycholesterol, 22R-hydroxycholesterol, 25-hydroxycholesterol, or pregnanolone, or an active portion of any one of 20S-hydroxycholesterol, 22S-hydroxycholesterol, 22R-hydroxycholesterol, 25-hydroxycholesterol, or pregnanolone.

26. The method of claim 24, wherein the at least one oxysterol is a combination of oxysterols selected from the group comprising 20S-hydroxycholesterol and 22R-hydroxycholesterol, or 20S-hydroxycholesterol and 22S-hydroxycholesterol.

27. The method of claim 25, further comprising treating the patient with at least one secondary agent selected from the group comprising parathyroid hormone, sodium fluoride, insulin-like growth factor I, insulin-like growth factor II or transforming growth factor beta, at a therapeutically effective dose.

28. A method of claim 25, further comprising treating a patient with at least one secondary agent selected from the group comprising bisphosphonates, selective estrogen receptor modulators, calcitonin, or vitamin D and calcium, at a therapeutically effective dose.

29. A method of treating a patient to induce bone formation comprising:

harvesting mammalian mesenchymal stem cells;

treating the mammalian mesenchymal cells with at least one agent, wherein the at least one agent induces the mesenchymal stem cells to express at least one cellular marker of osteoblastic differentiation;

administering the differentiated cells to the patient.

30. The method of claim 29, wherein the at least one oxysterol is selected from the group comprising 20S-hydroxycholesterol, 22S-hydroxycholesterol, 22R-hydroxycholesterol, 25-hydroxycholesterol, or pregnanolone, or an active portion of any one of 20S-hydroxycholesterol, 22S-hydroxycholesterol, 22R-hydroxycholesterol, 25-hydroxycholesterol, or pregnanolone.

31. The method of claim 29, wherein the at least one oxysterol is a combination of oxysterols selected from the group comprising 20S-hydroxycholesterol and 22R-hydroxycholesterol, or 20S-hydroxycholesterol and 22S-hydroxycholesterol.

32. The method of claim 29 further comprising administering at least one oxysterol at a therapeutically effective dose in an effective dosage form at a selected interval.

33. The method of claim 29, further comprising treating the patient with at least one secondary agent selected from the group comprising parathyroid hormone, sodium fluoride, insulin-like growth factor I, insulin-like growth factor II or transforming growth factor beta, at a therapeutically effective dose.

34. The method of claim 29, further comprising treating a patient with at least one secondary agent selected from the group comprising bisphosphonates, selective estrogen receptor modulators, calcitonin, or vitamin D and calcium, at a therapeutically effective dose.

35. The method of claim 29, further comprising administering the differentiated cells to the patient by systemic injection.

36. The method of claim 29, further comprising administering the differentiated cells to the patient by application of the cells to a selected site where bone formation is desired.

37. An implant for use in the human body comprising, a substrate having a surface, wherein at least the surface of the implant includes at least one oxysterol in an amount sufficient to induce bone formation in the surrounding bone tissue.

38. The implant of claim 37, wherein the substrate is formed into the shape of a pin, screw, plate, or prosthetic joint.

39. An implant for use in the human body comprising, a substrate having a surface, wherein at least the surface of the implant includes mammalian cells capable of osteoblastic differentiation.

40. An implant for use in the human body comprising, a substrate having a surface, wherein at least the surface of the implant includes osteoblastic mammalian cells.

41. A medicament for use in the treatment of bone disorders comprising a therapeutically effective dosage of at least one oxysterol selected from the group comprising 20S-hydroxycholesterol, 22S-hydroxycholesterol, 22R-hydroxycholesterol, 25-hydroxycholesterol, or pregnanolone, or an active portion of any one of 20S-hydroxycholesterol, 22S-hydroxycholesterol, 22R-hydroxycholesterol, 25-hydroxycholesterol, or pregnanolone.